GUIDELINES

European S3-Guidelines on the systemic treatment of psoriasis vulgaris – Update 2015 – Short version – EDF in cooperation with EADV and IPC

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Conflicts of interest

All authors declared their potential conflicts of interest. A detailed list is available in the methods report (DOI: 10.1111/jdv.13353).

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Introduction

This is an executive summary of all consented recommendations of the European Psoriasis Guidelines – Update 2015. The long version of this guideline is available online as supplementary file. A detailed description of the used methodology can be found in the methods report (DOI: 10.1111/jdv.13353).

In brief, available evidence of the efficacy and safety of the systemic treatments for psoriasis including an assessment of the quality of evidence was summarized using GRADE (Grading of Recommendations Assessment, Development and Evaluation).[1] The end of the literature search was October 12th, 2014. Some parts of the guidelines are based on a complete literature review (marked as evidence based), other parts are based on expert consensus only (marked as expert opinion). All recommendations (highlighted in grey) were formulated and consented by an expert panel, officially nominated by the European Dermatology Forum (EDF), the European Association for Dermatology and Venereology (EADV) or the International Psoriasis Council (IPC).

Table 1 Strength of recommendations: wording, symbols and implications[4,5]

Strength	Wording	Symbol
Strong recommendation **for** the use of an intervention	'We recommend . . .'	↑↑
Weak recommendation **for** the use of an intervention	'We suggest . . .'	↑
No recommendation with respect to an intervention	'We cannot make a recommendation with respect to . . .'	o
Weak recommendation **against** the use of an intervention	'We suggest not . . .'	↓
Strong recommendation **against** the use of an intervention	'We recommend not . . .'	↓↓

For the chapters of 'Special considerations and special patient populations', the literature was not systematically assessed and the recommendations are based on expert opinion only.

All recommendations were consented using formal consensus methodology (Delphi process or consensus conference with nominal group technique).[2,3] Based on the GRADE approach, the strength of recommendation is expressed by the wording and symbols shown in Table 1.

For each recommendation, the strength of consensus in terms of percentage of agreement was measured and documented. Three levels of consensus were defined and distinguished: 'strong consensus' (agreement of >90% of the members of the expert group), 'consensus' (75–89% agreement) and 'weak consensus' (50–74% agreement).

The guidelines have a validity until 31.12.2019.

Conventional systemic therapy

Acitretin

Instructions for use

Pre-treatment

- Objective assessment of the disease (such as PASI/BSA/PGA; arthritis)
- HRQoL (such as DLQI/Skindex-29 or -17)
- History and clinical examination should focus on musculoskeletal problems. If patient reports complaints, further imaging investigation may be performed
- Exclude pregnancy/breastfeeding: patient must be informed explicitly and extensively about the teratogenic risk of the medication, the necessity of effective long-term contraception (at least two years after cessation of treatment) and the possible consequences of a pregnancy while taking retinoids; written documentation of this informational interview
- Note that during and up to one year after treatment, blood donation is not permitted
- Laboratory controls (see Table 2)

During treatment

- Objective assessment of the disease (such as PASI/BSA/PGA; arthritis)
- HRQoL (such as DLQI/Skindex-29 or -17)
- Take capsules with a fatty meal or with whole milk
- Avoidance of pregnancy is mandatory. Start treatment on second or third day of the menstrual cycle, after satisfactory contraception for at least one month prior to treatment. Double contraception is recommended (e.g. condom + pill; IUD/Nuva Ring + pill; cave: no low-dosed progesterone preparations/mini-pills) during and up to two years after the end of therapy; effectiveness of oral contraceptives is reduced by acitretin
- Avoidance of alcohol
- Ask patient about spine and joint complaints at follow-up visits. If patient reports complaints, further imaging investigation may be performed
- Laboratory controls (see Table 2)

Post-treatment

- Reliable contraception in women of child-bearing age for up to two years after therapy, double contraception, as described above, is recommended
- Patients may not donate blood for up to one year after the discontinuation of therapy

Table 2 Recommended lab controls – acitretin

Parameter	Period in weeks						
	Pre-treatment	1	2	4	8	12	16
Blood count*	x				x		x
Liver enzymes**	x			x	x		
Serum creatinine	x						
Pregnancy test (urine)	x	Monthly up to 2 years after therapy (see national regulations)					
Fasting blood glucose	x						
Triglycerides, cholesterol, HDL	x			x			x
Not all tests may be necessary for all patients. Patient history, risk exposure and patient characteristics have to be taken into account. Further specific testing may be required according to clinical signs, risk and exposure.							

*Hb, Hct, leucocytes, platelets.
**AST, ALT, AP, γGT.

Therapeutic recommendations

Recommendation		Strength of consensus	Comment
Based on the available evidence we cannot make a recommendation for or against the use of acitretin as a monotherapy.	o	Consensus	Evidence and consensus based
Based on clinical experience and depending on the most important outcome for the individual patient, we suggest a low dose (20–30 mg daily) with respect to tolerability and a high dose (>30 mg daily) with respect to efficacy.	↑	Consensus	Expert opinion

Therapeutic combinations

Recommendation		Strength of consensus	Comments
Adalimumab	o	Consensus	No evidence available
Ciclosporin	↓	Strong consensus	Expert opinion: competition cytochrome P450 inactivation
Etanercept	↑	Consensus	Expert opinion: good safety profile assumed, possibly increased efficacy
Fumaric acid esters	o	Consensus	No evidence available
Infliximab	o	Consensus	No evidence available
Methotrexate	↓	Strong consensus	Expert opinion: increased risk of hepatotoxicity possible
Ustekinumab	o	Consensus	No evidence available

Ciclosporin

Instructions for use
Pre-treatment • Objective assessment of the disease (such as PASI/BSA/PGA; arthritis) • HRQoL (such as DLQI/ Skindex-29 or -17) • History and clinical examination should focus on previous and concomitant diseases (e.g. arterial hypertension; severe infections; malignancies, including cutaneous malignancies; renal and liver diseases) and concomitant medication (see Drug interactions, long version) • Measurement of blood pressure on two separate occasions • Laboratory controls (see Table 3) • Reliable contraception (cave: reduced efficacy of progesterone-containing contraceptives) • Regular gynaecologic screening according to national guidelines • Consultation on vaccination; susceptibility to infections (take infections seriously, seek medical attention promptly); drug interactions (inform other treating physicians about therapy); avoidance of excessive sun exposure; use of sunscreens *During treatment* *In uncomplicated long-term therapy with low-dose ciclosporin (CSA; 2.5–3 mg/kg daily), follow-up intervals may be extended to two months or more. Shorter intervals may be needed in patients with risk factors, dose increases, or those who must take concomitant medications that are likely to contribute to ADR. In selected patients with intermittent and short-term treatment, less strict monitoring (regular checking of blood pressure and creatinine level) may be sufficient.* • Objective assessment of the disease (such as PASI/BSA/PGA; arthritis) • HRQoL (such as DLQI/Skindex-29 or -17) • Clinical examination should focus on the status of skin and mucous membranes (hypertrichosis, gingival changes), signs of infections, gastrointestinal or neurological symptoms (tremor, dysaesthesia) and musculoskeletal/joint pain • Repeat recommendation for sun avoidance and sun protection • Check of concomitant medication • Measurement of blood pressure • Laboratory controls (see Table 3) • Reliable contraception • Regular gynaecologic screening according to national guidelines • If creatinine is significantly elevated and/or patient on therapy for >1 year, perform creatinine clearance (or creatinine-EDTA clearance where available). • Determination of the CSA level is recommended in individual cases. *Post-treatment* • After discontinuation of CSA, patients should be followed up for skin cancer, especially in case of extensive prior therapeutic or natural UV exposure.

Table 3 Recommended lab controls – ciclosporin

Diagnostics	Period in weeks					
	Pre-treatment	2	4	8	12	16
Full blood count*	x	x	x	x	x	x
Liver values**	x	x	x	x	x	x
Electrolytes***	x	x	x	x	x	x
Serum creatinine	x	x	x	x	x	x
Urine status	x		x			x
Uric acid	x		x	x	x	x
Pregnancy test (urine)	x					
Cholesterol, triglycerides	x****			x		x
Magnesium*****	x			x		x
HBV/HCV	x					
HIV	x					
Not all tests may be necessary for all patients. Patient history, risk exposure and patient characteristics have to be taken into account. Further specific testing may be required according to clinical signs, risk and exposure.						

*Erythrocytes, leucocytes, platelets.
**Transaminases, AP, γGT, bilirubin.
***Sodium, potassium.
****Recommended two weeks before and on the day of treatment initiation (fasting).
*****Only with indication (muscle cramps).

Therapeutic recommendations

Recommendation		Strength of consensus	Comment
If a short course for induction treatment is intended we recommend CSA.	↑↑	Strong consensus	Evidence and consensus based
For long-term treatment we suggest CSA only in selected patients.	↑	Strong consensus	Expert opinion
In case of continuous long-term treatment, we suggest CSA for a maximum of up to two years.	↑	Consensus	Expert opinion
In case a longer treatment is needed, we suggest the consultation with a nephrologist.	↑	Consensus	Expert opinion
Based on weighting of risk and benefit we suggest using CSA with a starting dose of 2.5 mg/kg bodyweight QD for up to four weeks, with a dosage increase up to 5 mg/kg bodyweight once daily thereafter.	↑	Weak consensus	Evidence and consensus based

Therapeutic combinations

Recommendation		Strength of consensus	Comments
Acitretin	↓	Strong consensus	Expert opinion: competition cytochrome P450 inactivation
Adalimumab	↓	Consensus	Expert opinion: increased risk of immunosuppression
Etanercept	↓	Consensus	Expert opinion: increased risk of immunosuppression
Fumaric acid esters	o	Consensus	No evidence available
Infliximab	↓	Consensus	Expert opinion: increased risk of immunosuppression
Methotrexate	↓	Weak consensus	Expert opinion: increased risk of immunosuppression
Ustekinumab	↓	Consensus	Expert opinion: increased immunosuppression, anecdotal evidence of increased toxicity

Fumaric acid esters

Instructions for use

Pre-treatment

- Objective assessment of the disease (such as PASI/BSA/PGA; arthritis)
- HRQoL (such as DLQI/Skindex-29 or -17)
- History and clinical examination
- Laboratory controls (see Table 4)

During treatment

- Objective assessment of the disease (such as PASI/BSA/PGA; arthritis)
- HRQoL (such as DLQI/Skindex-29 or -17)
- Clinical examination
- Laboratory controls (see Table 4)

Post-treatment

- None.

Table 4 Recommended lab controls – fumaric acid esters

Parameter	Period in weeks			
	Pre-treatment	Month 1	Every 4 weeks until month 4	Thereafter
Liver enzymes	x	x	x	every 8 weeks
Serum creatinine	x	x	x	every 8 weeks
Urine status	x	x	x	every 8 weeks
Pregnancy test	x			
Blood count*	x	x	x	every 4 weeks**
Not all tests may be necessary for all patients. Patient history, risk exposure and patient characteristics have to be taken into account. Further specific testing may be required according to clinical signs, risk and exposure.				

*If leukocytes are <3000/μl, fumarate therapy needs to be stopped. If lymphocytes are <700/μl, patients should be kept on half of the last dose for 2–4 weeks and stopped if lymphocytes remain below 700/μl; if lymphocytes are <500/μl, treatment must be terminated.
**Frequency of lab control of blood count was a matter of debate, including repeated Delphi voting. No strong consensus was achieved, the recommendation passed with 'weak consensus' (63%).

Therapeutic recommendations

Recommendation		Strength of consensus	Comment
We recommend fumaric acid esters for the induction treatment.	↑↑	Consensus	Evidence and consensus based
We recommend fumaric acid esters for the long-term treatment.	↑↑	Consensus	Expert opinion
We recommend fumaric acid esters with a slow increase dosing regimen.	↑↑	Consensus	Expert opinion

Therapeutic combinations

Recommendation		Strength of consensus	Comments
Acitretin	o	Consensus	No evidence available
Adalimumab	o	Strong consensus	No evidence available
Ciclosporin	o	Consensus	No evidence available
Etanercept	o	Strong consensus	No evidence available
Infliximab	↓	Consensus	Expert opinion: increased risk of immunosuppression, lymphocytopenia
Methotrexate	↓	Consensus	Expert opinion: increased risk of immunosuppression
Ustekinumab	o	Consensus	No evidence available

Methotrexate

Instructions for use

Pre-treatment

- History and clinical examination
- Objective assessment of the disease (such as PASI/BSA/PGA; arthritis)
- HRQoL (such as DLQI/Skindex-29 or -17)
- Laboratory parameters (see Table 5)
- Chest X-ray
- Contraception in women of child-bearing age (starting after menstruation), and also in men
- If abnormalities in liver screening are found, refer patient to specialist for further evaluation

During treatment

- Objective assessment of the disease (such as PASI/BSA/PGA; arthritis)
- HRQoL (such as DLQI/Skindex-29 or -17)
- Check concomitant medication
- Clinical examination
- Laboratory controls (see Table 5)
- Contraception in women of child-bearing age, and also in men
- 5 mg folic acid once weekly, 24 h after MTX

Post-treatment

- Women must not become pregnant and men must not father a child for at least three months thereafter

Table 5 Recommended lab controls – methotrexate

Parameter	Period in weeks/months			
	Pre-treatment	After first week	During first two months, 1 × every 2 weeks	Thereafter, every 2–3 months
Blood count*	x	x	x	x
Liver enzymes	x		x	x
Serum creatinine	x		x	x
Urine status	x		x	x
Pregnancy test (urine)	x			
HBV/HCV	x			
HIV	x			
Serum albumin**	x		x	x
PIIINP where available	x		Every 3 months***	
Not all tests may be necessary for all patients. Patient history, risk exposure and patient characteristics have to be taken into account. Further specific testing may be required according to clinical signs, risk and exposure.				

*If blood leucocytes <3.0, neutrophils <1.0, thrombocytes <100, or liver enzymes >2 × baseline values, decrease the dose or discontinue the medication.
**In selected cases (e.g. in cases with suspected hypoalbuminaemia or in patients using other drugs with high binding affinity for serum albumin).
***Liver biopsy when necessary in selected cases; should be considered, for example, in patients with persistently abnormal PIIINP (>4.2 mcg/l in at least three samples over a 12-month period).

Therapeutic recommendations

Recommendation		Strength of consensus	Comment
We recommend MTX for the induction and long-term treatment.	↑↑	Strong consensus	Evidence and consensus based
Methotrexate can be given by oral or subcutaneous delivery. In general, a starting dose of 15 mg/week is used but individual dosages can range from 5 to 25 mg/week depending on individual factors.	Statement	Strong consensus	Expert opinion

Therapeutic combinations

Recommendation		Strength of consensus	Comments
Acitretin	↓	Strong consensus	Expert opinion: increased risk of hepatotoxicity possible
Adalimumab	↑	Consensus	Expert opinion: combination widely used in rheumatology; combination with low-dose MTX (e.g. 7.5–10 mg/week is likely sufficient to reduce formation of anti-drug antibodies (ADA) and increase trough levels of adalimumab)
Ciclosporin	↓	Weak consensus	Expert opinion: increased risk of immunosuppression
Etanercept	↑	Consensus	Evidence (additional benefit of adding MTX to etanercept compared to etanercept monotherapy) and consensus based
Fumaric acid esters	↓	Consensus	Expert opinion: increased risk of immunosuppression
Infliximab	↑	Consensus	Expert opinion: combination widely used in rheumatology; combination with low-dose MTX (e.g. 7.5–10 mg/week is likely sufficient to reduce formation of ADA and increase trough levels of infliximab)
Ustekinumab	o	Consensus	No evidence available

Biological therapy

Adalimumab

Instructions for use
Pre-treatment • Physicians are encouraged to enrol their patients in a registry (if available) • Objective assessment of the disease (such as PASI/BSA/PGA; arthritis) • HRQoL (such as DLQI/Skindex-29 or -17) • History and clinical examination should focus on prior exposure to treatments, malignancies, infections, congestive heart failure (CHF) and neurological disease or symptoms • Recommended measures include: - Check for skin cancer - Check for lymphadenopathy - Laboratory parameters (see Table 6) - Exclusion of tuberculosis (see chapter 5.1 in long version) - Check for evidence of active infection • Contraception *During treatment* • Objective assessment of the disease (such as PASI/BSA/PGA; arthritis) • HRQoL (such as DLQI/Skindex-29 or -17) • Clinical examination should focus on malignancies, risk factors for serious infections, congestive heart failure and neurological symptoms • Recommended measures include: - Check for skin cancer - Check for lymphadenopathy - Laboratory parameters (see Table 6) • Contraception *Post-treatment* • After discontinuation of adalimumab, patients should be followed up with medical history and physical examination • Reliable contraception until five months after treatment, if applicable (according to the label)

Table 6 Recommended lab controls – adalimumab

Parameter	Period in weeks			
	Pre-treatment	4	12	Thereafter, every 3–6 months
Full blood count	x	x	x	x
Liver enzymes	x	x	x	x
Serum creatinine	x	x	x	x
Urine status	x	x	x	x
Pregnancy test (urine)	x			
CRP	x			
HBV/HCV	x			
HIV	x			
Not all tests may be necessary for all patients. Patient history, risk exposure and patient characteristics have to be taken into account. Further specific testing may be required according to clinical signs, risk and exposure.				

Therapeutic recommendations

Recommendation		Strength of consensus	Comment
We recommend adalimumab as second-line medication* for the induction and long-term treatment.	↑↑	Strong consensus	Evidence and consensus based
We recommend using adalimumab with an initial loading dose of 80 mg for week 1, followed by 40 mg every other week.	↑	Strong consensus	Expert opinion

*If phototherapy and conventional systemic agents were inadequate in response or if they are contraindicated or not tolerated.

Therapeutic combinations

Recommendation		Strength of consensus	Comments
Acitretin	o	Consensus	No evidence available
Ciclosporin	↓	Consensus	Expert opinion: increased risk of immunosuppression
Fumaric acid esters	o	Strong consensus	No evidence available
Methotrexate	↑	Consensus	Expert opinion: combination widely used in rheumatology; combination with low-dose MTX (e.g. 7.5–10 mg/week is likely sufficient to reduce formation of ADA and increase trough levels of adalimumab)
Ustekinumab	↓	Consensus	Expert opinion: increased risk of immunosuppression

Etanercept

Instructions for use

Pre-treatment

- Physicians are encouraged to enrol their patients in a registry (if available)
- Objective assessment of the disease (such as PASI/BSA/PGA; arthritis)
- HRQoL (such as DLQI/Skindex-29 or -17)
- History and clinical examination should focus on prior exposure to treatments, malignancies, infection, congestive heart failure and neurological symptoms
- Recommended measures include:
  - Check for malignancy, mainly skin cancer and pre-malignant lesions
  - Check for lymphadenopathy
  - Laboratory parameters (see Table 7)
  - Exclusion of tuberculosis (see chapter 5.1 in long version)
  - Check for evidence of active infection
- Contraception

During treatment

- Objective assessment of the disease (such as PASI/BSA/PGA; arthritis)
- HRQoL such as (DLQI/Skindex-29 or -17)
- Clinical examination should focus on lymphadenopathy, malignancies, especially skin cancer, premalignant lesions, risk factors for serious infections, congestive heart failure and neurological symptoms
- Recommended measures include:
  - Laboratory parameters (see Table 7)
- Contraception

Post-treatment

- After discontinuation of etanercept, patients should be followed up with medical history and physical examination.
- Women of childbearing potential should be advised to use appropriate contraception to avoid becoming pregnant for three weeks after discontinuation of therapy.

Table 7 Recommended lab controls – etanercept

Parameter	Period in weeks			
	Pre-treatment	4	12	Thereafter, every 3–6 months
Full blood count	x	x	x	x
Liver enzymes	x	x	x	x
Serum creatinine	x	x	x	x
Urine status	x			
Pregnancy test (urine)	x			
CRP	x			
HBV/HCV	x			
HIV	x			

Not all tests may be necessary for all patients. Patient history, risk exposure and patient characteristics have to be taken into account. Further specific testing may be required according to clinical signs, risk and exposure.

Therapeutic recommendations

Recommendation		Strength of consensus	Comment
We recommend etanercept as second-line* medication for the induction and long-term treatment.	↑↑	Strong consensus	Evidence and consensus based
In general, a starting dose of 50 mg once or twice weekly is used depending on individual factors.	Statement	Strong consensus	Expert opinion
For maintenance therapy 50 mg once weekly is a commonly used dose.	Statement	Strong consensus	Expert opinion

*If phototherapy and conventional systemic agents were inadequate in response or if they are contraindicated or not tolerated.

Therapeutic combinations

Recommendation		Strength of consensus	Comments
Acitretin	↑	Consensus	Expert opinion: good safety profile assumed, possibly increased efficacy
Ciclosporin	↓	Consensus	Expert opinion: increased risk of immunosuppression
Fumaric acid esters	o	Strong consensus	No evidence available
Methotrexate	↑	Consensus	Evidence (additional benefit of adding MTX to etanercept compared to etanercept monotherapy) and consensus based
Ustekinumab	↓	Consensus	Expert opinion: increased risk of immunosuppression

Infliximab

Instructions for use

Pre-treatment

- Physicians are encouraged to enrol their patients in a registry (if available)
- Objective assessment of the disease (such as PASI/BSA/PGA; arthritis)
- HRQoL (such as DLQI/Skindex-29 or -17)
- History focusing on prior exposure to treatments. History and clinical examination should focus on malignancies, infection, congestive heart failure and neurological symptoms
- Recommended measures include:
  - Check for skin cancer
  - Check for lymphoadenopathy
  - Laboratory parameters (see Table 8)
  - Exclusion of tuberculosis (see chapter 5.1 in long version)
  - Check for evidence of active infection
- Contraception

During treatment

- Objective assessment of the disease (such as PASI/BSA/PGA; arthritis)
- HRQoL (such as DLQI/ Skindex-29 or -17)
- Clinical examination should focus on malignancies, risk factors for serious infections, congestive heart failure and neurological symptoms
- Recommended measures include:
  - Check for skin cancer
  - Check for lymphoadenopathy
  - Laboratory parameters (see Table 8)
- Contraception

Post-treatment

- After discontinuation of infliximab, patients should be followed up with medical history and physical examination

Table 8 Recommended lab controls – infliximab

Parameter	Period in weeks			
	Pre-treatment	2	6	Thereafter, prior to each infusion
Full blood count	x	x	x	x
Liver enzymes	x	x	x	x
Serum creatinine	x	x	x	x
Urine status	x	x	x	x
Pregnancy test (urine)	x			
CRP	x			
HBV/HCV	x			
HIV	x			
Not all tests may be necessary for all patients. Patient history, risk exposure and patient characteristics have to be taken into account. Further specific testing may be required according to clinical signs, risk and exposure.				

Therapeutic recommendations

Recommendation		Strength of consensus	Comment
We recommend infliximab as second-line* medication for the induction and long-term treatment.	↑↑	Strong consensus	Evidence and consensus based
We recommend using infliximab 5 mg/kg bodyweight continuously every eight weeks during long-term treatment.	↑↑	Strong consensus	Evidence and consensus based

*If phototherapy and conventional systemic agents were inadequate in response or if they are contraindicated or not tolerated.

Therapeutic combinations

Recommendation		Strength of consensus	Comments
Acitretin	o	Consensus	No evidence available
Ciclosporin	↓	Consensus	Expert opinion: increased risk of immunosuppression
Fumaric acid esters	↓	Consensus	Expert opinion: increased risk of immunosuppression, lymphocytopenia
Methotrexate	↑	Consensus	Expert opinion: combination widely used in rheumatology; combination with low-dose MTX (e.g. 7.5–10 mg/week is likely sufficient to reduce formation of ADA and increase trough levels of infliximab)
Ustekinumab	↓	Consensus	Expert opinion: increased risk of immunosuppression

Ustekinumab

Instructions for use

Pre-treatment

- Physicians are encouraged to enrol their patients in a registry (if available)
- Objective assessment of disease (such as PASI/BSA/PGA; arthritis)
- HRQoL (such as DLQI/Skindex-29 or -17)
- History and clinical examination focusing on previous treatment exposure, UV light, malignancies, infections
- Recommended measures include:
  - Check for skin cancer
  - Check for lymphadenopathy
  - Laboratory parameters (see Table 9)
  - Exclusion of tuberculosis (see chapter 5.1 in long version)
  - Evaluation of comorbidities including cardiovascular risk factors
  - Check for evidence of active infection
- Contraception

During treatment

- Objective assessment of disease (such as PASI/BSA/PGA; arthritis)
- Patient oriented outcomes such as pruritus, DLQI and Skindex-29 or -17
- History and clinical examination focusing on malignancies and infections
- Recommended measures include:
  - Check for skin cancer and lymphadenopathy
  - Pregnancy
  - Evaluation of treatment adherence

Post-treatment

- Patients should be followed up with medical history and clinical examination
- Contraception to be maintained for 15 weeks

Table 9 Recommended lab controls – ustekinumab

Parameter	Period in weeks/months	
	Pre-treatment	Thereafter every 3–6 months
Full blood count	x	x
Liver enzymes	x	x
Serum creatinine	x	x
Urine status	x	x
Pregnancy test (urine)	x	
CRP	x	
HBV/HCV	x	
HIV	x	

Not all tests may be necessary for all patients. Patient history, risk exposure and patient characteristics have to be taken into account. Further specific testing may be required according to clinical signs, risk and exposure.

Therapeutic recommendations

Recommendation		Strength of consensus	Comment
We recommend ustekinumab as second-line medication* for the induction and long-term treatment.	↑↑	Strong consensus	Evidence and consensus based
We suggest using 45 mg for patients with a bodyweight of ≤100 kg and 90 mg ustekinumab for patients with a bodyweight of >100 kg.	↑	Strong consensus	Evidence and consensus based

*if phototherapy and conventional systemic agents were inadequate in response or if they are contraindicated or not tolerated (the label currently states: if PUVA or other systemic therapies including ciclosporin, methotrexate were inadequate in response or if they are contraindicated or not tolerated). No strong consensus on definition of 'second-line' for ustekinumab was achieved, the definition passed with 'weak consensus' (55%).

Therapeutic combinations

Recommendation		Strength of consensus	Comments
Acitretin	o	Consensus	No evidence available
Adalimuab	↓	Consensus	Expert opinion: increased risk of immunosuppression
Ciclosporin	↓	Consensus	Expert opinion: increased immunosuppression, anecdotal evidence of increased toxicity
Etanercept	↓	Consensus	Expert opinion: increased risk of immunosuppression
Fumaric acid esters	o	Consensus	No evidence available
Infliximab	↓	Consensus	Expert opinion: increased risk of immunosuppression
Methotrexate	o	Consensus	No evidence available

Special considerations and special patient populations

Tuberculosis (TB) screening before and during biologic treatment

Recommendation		Strength of consensus	Comment
We recommend to do tuberculosis screening according to local regulations.	↑↑	Strong consensus	Expert opinion
For pre-screening, we recommend anamnesis including tuberculosis history; a chest X-ray; TST and/or IGRA.	↑↑	Strong consensus	Expert opinion
We recommend remaining alert to the possibility of tuberculosis infection during therapy. This includes taking medical history and might include tuberculosis testing.	↑↑	Strong consensus	Expert opinion

Hepatitis/other hepatological dysfunctions

Recommendation		Strength of consensus	Comment
We recommend to screen patients for hepatitis B and hepatitis C before starting treatment with a biologic or methotrexate.	↑↑	Consensus	Expert opinion
We recommend to screen patients for hepatitis B before starting treatment with ciclosporin.	↑↑	Consensus	Expert opinion
If a positive marker is found, or the patient is known to have had prior infection we recommend to consult a gastroenterologist with an interest in hepatology.	↑↑	Weak consensus	Expert opinion
We recommend to record all cases of reactivation/ exacerbation via drug registries.	↑↑	Consensus	Expert opinion

HIV

Recommendation		Strength of consensus	Comment
We recommend the combination of anti-retroviral therapy with topical therapies (steroids, vitamin D derivatives, or combination of both) as first-line treatment strategy for mild to moderate psoriasis in HIV-infected patients.	↑↑	Strong consensus	Expert opinion
For moderate-to-severe psoriasis, we recommend highly active anti-retroviral therapy with skin-directed therapies, e.g. topicals and/or phototherapy (narrowband UVB mainly) as first-line strategy.	↑↑	Strong consensus	Expert opinion
We suggest acitretin as second-line treatment in addition to highly active anti-retroviral therapy.	↑	Strong consensus	Expert opinion
We suggest using methotrexate or ciclopsorin or biologics only in patients with severe, refactory psoriasis with well controlled HIV disease using HAART, in collaboration with a specialist on HIV medicine.	↑	Strong consensus	Expert opinion
In cases showing lack of response, intolerance, or contraindication to conventional systemic immunosuppressants, we suggest to consider biologics.	↑	Consensus	Expert opinion
We suggest using etanercept as biologic of choice in patients with severe, refactory psoriasis with well controlled HIV disease using HAART.	↑	Consensus	Expert opinion

Malignancies including lymphoma and skin cancer

Recommendation		Strength of consensus	Comment
For patients with recent malignancy we recommend topical therapies, phototherapy (narrow band UVB) * and/or acitretin. *except cutaneous malignancies	↑↑	Strong consensus	Expert opinion
In case of inadequate response to topical therapies, phototherapy, (narrow band UVB) and/or acitretin we suggest using MTX.	↑	Consensus	Expert opinion
We recommend to discuss the decision to initiate immunosuppressive therapies, in psoriasis patients with a current or recent diagnosis of cancer in the previous five years case by case with cancer specialists and to reach an informed decision, respecting the patient's preference.	↑↑	Consensus	Expert opinion
The elements to be taken into account for the shared decision are the type and staging of cancer, the risk of recurrence and the burden of psoriasis in the individual patient.	Statement	Strong consensus	Expert opinion
In some cancers with relatively good prognosis, where flares of psoriasis cannot be controlled by other therapies, we suggest to consider earlier introduction of immunosuppressive therapies. In this case, we suggest methotrexate as the preferred systemic agent to be used.	↑	Strong consensus	Expert opinion
In patients with concurrent cancer treatment who are treated with immunosuppressive agents, we recommend to perform a search for pharmacological interactions in coordination with the oncologist.	↑↑	Consensus	Expert opinion

Neurological disease

Recommendation		Strength of consensus	Comment
We do not recommend TNF antagonist therapy in people with diagnosis of multiple sclerosis or other demyelinating disease.	↓↓	Strong consensus	Expert opinion
We recommend caution using TNF antagonist therapy in people with a first degree relative with multiple sclerosis or other demyelinating disease.	↑↑	Strong consensus	Expert opinion
We suggest choosing fumaric acid esters in people with multiple sclerosis.	↑	Strong consensus	Expert opinion

Ischaemic heart disease and congestive heart failure

Recommendation		Strength of consensus	Comment
We recommend not using CSA as a first-line treatment in patients with arterial hypertension.	↓↓	Strong consensus	Expert opinion
We suggest not using TNF antagonists in subjects with NHHA class III or IV congestive heart failure.	↓	Consensus	Expert opinion

Diabetes mellitus

Recommendation		Strength of consensus	Comment
We suggest not using ciclosporin as a first-line treatment in patients with diabetes and/or features of the metabolic syndrome.	↓	Consensus	Expert opinion
We suggest not using acitretin as a first-line treatment in patients with dyslipidaemia.	↓	Consensus	Expert opinion

Kidney failure/Renal impairment

Recommendation		Strength of consensus	Comment
We recommend ensuring an accurate assessment of renal function in any patient with known or suspected chronic kidney disease prior to therapy.	↑↑	Strong consensus	Expert opinion
We recommend working in collaboration with the nephrologist when prescribing systemic therapy in any patient with chronic kidney disease of stage 3 or more.	↑↑	Strong consensus	Expert opinion
We suggest using methotrexate, acitretin, or biological therapy in people with chronic kidney disease stage 2–3.	↑	Consensus	Expert opinion
We recommend using a reduced dose of methotrexate in people with chronic kidney disease stage 3.	↑↑	Consensus	Expert opinion
In people with chronic kidney disease stage 4–5 biologics can be used.	Statement	Strong consensus	Expert opinion
We recommend not using ciclosporin or fumaric acid esters in chronic kidney disease stage 3 or more.	↓↓	Strong consensus	Expert opinion
We recommend not using methotrexate in chronic kidney disease 4 or 5.	↓↓	Strong consensus	Expert opinion

Wish for pregnancy in near future

Recommendation		Strength of consensus	Comment
We recommend to advise the use of topical emollients, and low to moderate strength corticosteroids of short duration as first-line therapy in women with a wish for pregnancy in the near future or who are pregnant.	↑↑	Consensus	Expert opinion
We recommend phototherapy with narrow band UVB for women who are inadequately controlled by emollients and topical steroids who wish to become pregnant or who are pregnant.	↑↑	Strong consensus	Expert opinion
For pregnant women with severe psoriasis requiring systemic therapy for which the benefits outweigh the risk, we suggest to consider etanercept.	↑	Strong consensus	Expert opinion
We recommend not using acitretin and methotrexate in women considering becoming pregnant or who are pregnant.	↓↓	Consensus	Expert opinion

Psoriatic arthritis

Recommendation		Strength of consensus	Comment
For relief of symptoms of psoriatic arthritis, we recommend NSAIDs. As a monotherapy, we recommend NSAIDs for patients with mild and non-erosive articular as well as para-articular involvement.	↑↑	Strong consensus	Expert opinion
In patients with active joint involvement despite the usage of NSAIDs and potential poor prognosis due to polyarthritis, increased inflammatory markers and erosive changes, we recommend to start synthetic DMARDs early to prevent progression of disease and erosive destruction of joints.	↑↑	Consensus	Expert opinion
For inadequately responding patients after at least one synthetic DMARD, we recommend the use of biological DMARDs in combination with synthetic DMARDs or as monotherapy.	↑↑	Consensus	Expert opinion
We do not recommend synthetic monotherapy DMARDs for the treatment of axial involvement or enthesitis, as they appear to be not effective in these patients.	↓↓	Strong consensus	Expert opinion

Newly approved medications and treatments in the pipeline

The field of psoriasis treatments is evolving rapidly and several new treatments have been developed. For any guideline, it is a challenge to be up to date with the rapidly changing market of psoriasis treatments. New medications with very little use during regular clinical practice are difficult to assess with expert opinion knowledge. The guideline group has decided to focus on the licensed treatment options at the time point of the consensus conference. The group decided against a prospective inclusion of new drugs that are likely to be licensed in the near future, especially also in the light of lack of expert experience with these new drugs.

Since the cut off date for inclusion of approved medications in Europe (October 2014), secukinumab and apremilast have been granted market authorization by EMA.[6,7] An update including newly approved medications is currently under preparation.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Data S1. Long version: European S3-Guidelines on the systemic treatment of psoriasis vulgaris – update 2015 – EDF in cooperation with EADV and IPC.